

**ENVIRONMENTAL MAGNESIUM SUPPLY, MUTATION OF ION CHANNELS
AND TRANSPORTERS****Zoltan Kiss***Department of Medicine CSMEK Hódmezővásárhely-Makó H6900 Makó, Kórház u. 2.***Abstract**

Decreasing Mg-content of soil and foods aren't an isolate phenomenon. It is inseparable from the effect of other ions (1). Beside deterioration of ion equilibrium, the property of accumulation of toxic metals due to global environmental pollution is very disadvantageous, because these can substitute vital, essential macro- and microelements and can competitively block transporters and channels. The unfavorable effect are strengthened by mutations of transporters and channels, which may be the causes of severe immunodeficiencies, life-threatening arrhythmias as background of frequent diseases and do have significant public health impact via widespread use and results of genetic tests.

Introduction

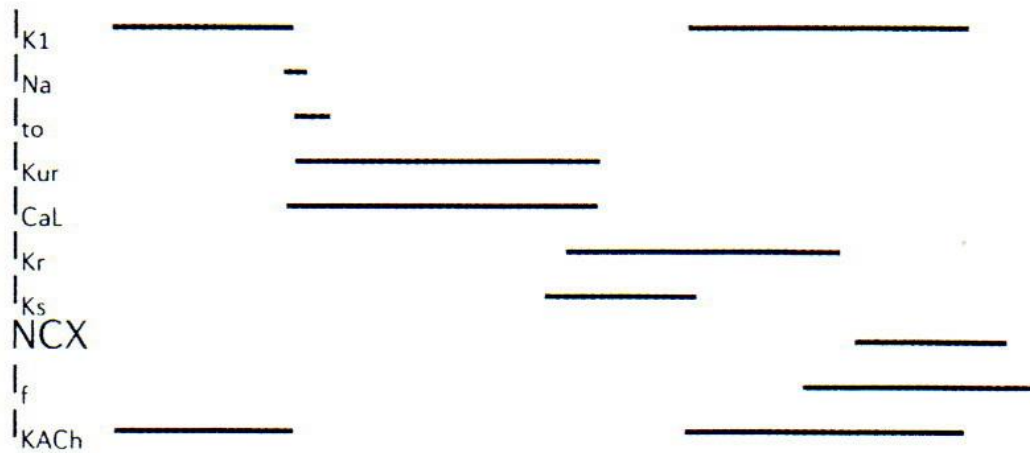
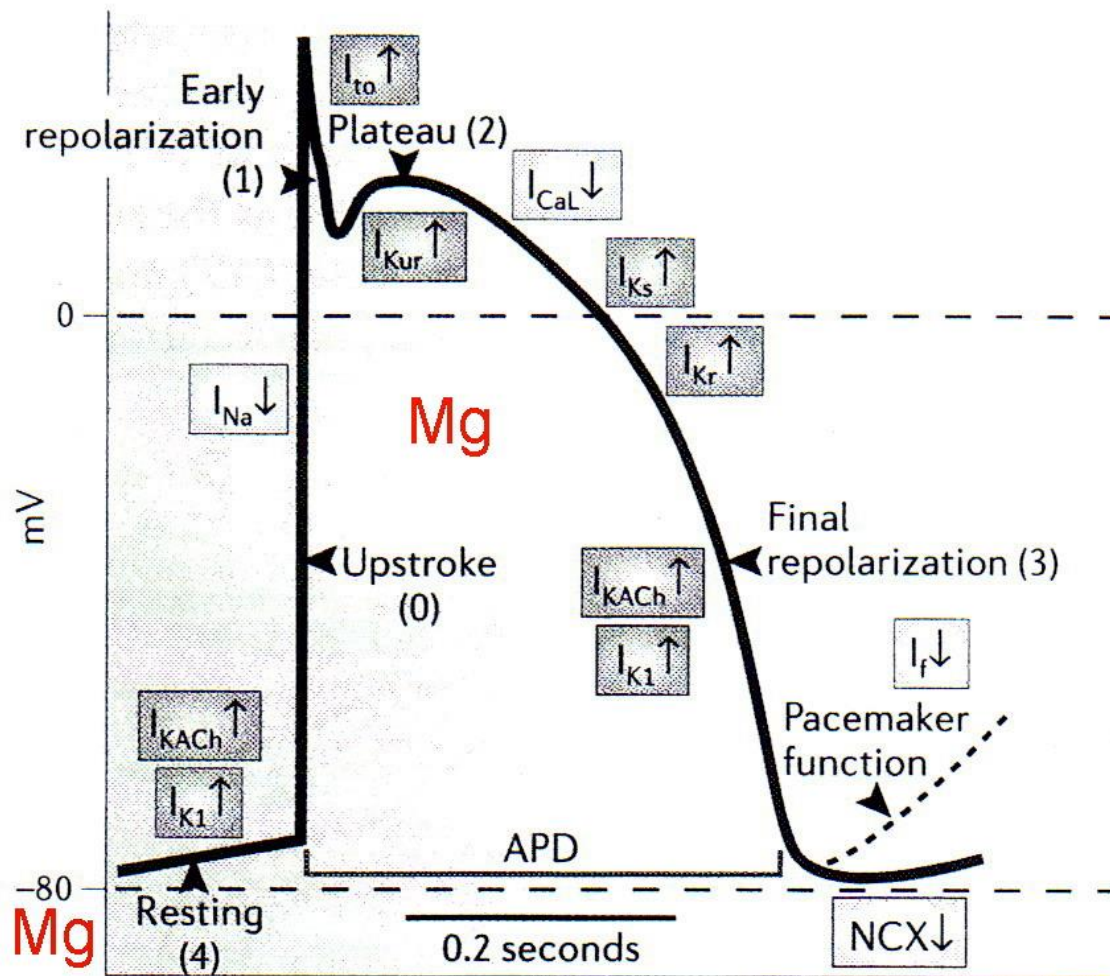
Decreasing Mg-content of soil and foods isn't an isolate phenomenon. It is inseparable from the effects of other ions, which are important signaling cations in immun system (2).

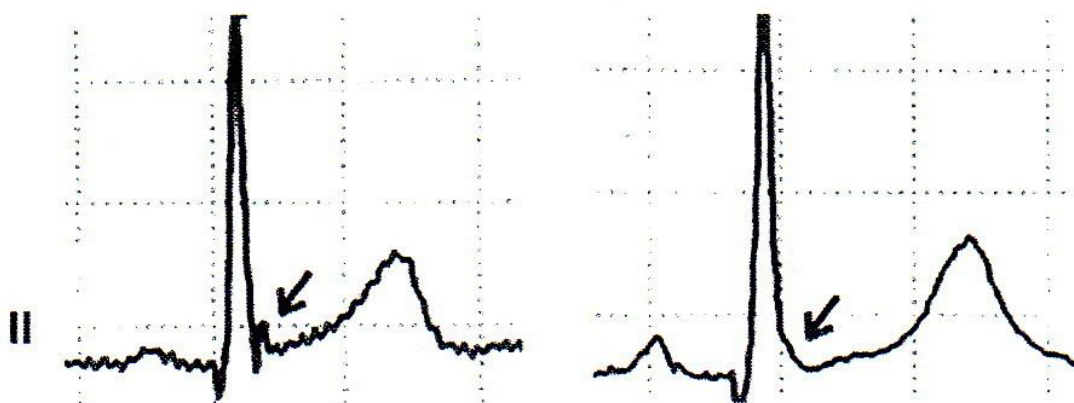
Beside deterioration of ion equilibrium, the property of accumulation of toxic metals due to global environmental pollution is very disadvantageous, because these can substitute vital, essential macro- and microelements and can competitively block transporters and channels.

Human and experimental data

Loss of function mutations in the gene encoding in MAGT1-as a critical regulator of intracellular free Mg^{++} level- cause XMEN disease with X-linked combined immunodeficiency with magnesium defect. It's characterised by CD4 lymphopenia, chronic Epstein-Barr virus (EBV) infection and related lymphoproliferative disorders (e.g lymphoma). Oral magnesium L-threonate led to better control of EBV infection. There are mutations in SCN5A sodium channel and A109A genes (3) increases the outward transient K-flux (Ito), which regulated by magnesium (4). The early repolarization was experimentally evoked by us (5).

Fig.1 demonstrates the action potentials of myocardial fiber with early transient K-efflux (a), spike and dome and early ventricular repolarization signs (b) on human surface ECG unipolar leads (arrows).





In J-wave syndromes with episodes of ventricular fibrillation (Brugada and early repolarisation syndrome, (6), was no association between serum K^+ or Ca^{++} and repolarisation, but there was a significant negative correlation between serum Mg^{++} and repolarisation dispersion (7).

The non-selective calcium-activated transient receptor potential channels are activated by receptor, ligand or direct mode and one of them (TPRM7) is taking part in the regulation of Mg-homeostasis (8). TRPM6 gene mutation leads to autosomal recessive hypomagnesemia and hypocalcemia (9). At the same time, Mg blocks the excessive Ca and environmental toxic metals' (Zn,Co,Ni,Ba,Pb,10) influx. In the case of mutation, the intracellular Ca-influx increases in malignant tumors, supporting progression.

Discussion

There is an overlap in phenotype and electrophysiological similarities between Brugada syndrome and early repolarization (11). The presence of a prominent I_{to} -mediated action potential notch (spike and dome) in the epicardium, but not the endocardium, generates a transmural voltage gradient during the early phase of repolarization, which manifests J-wave and J-point elevation in the surface ECG in both ERP and Brugada syndrome. Heterogeneous loss of the action potential dome produces phase 2 reentry, leading to polymorphic ventricular tachycardia/ventricular fibrillation. Mutation of paracellin-1 manifests in hypomagnesemic-hypercalcuric- syndrome. Mg homeostasis plays a very important role in prevention of serious consequences of hypomagnesemia. It is inseparable from the actions of other ions.

Conclusion

The above-mentioned mutations may be the causes of severe immunodeficiencies, life-threatening arrhythmias as background of frequent diseases (recurrent sinopulmonary infections, pneumonias, syncope) and do have significant public health impact via widespread use of genetic tests in the future. Of note that blocking the intracellular influx of toxic environmental metals may have a role in the planning of medicines will be developed for the treatment of civilization disorders, e.g. hypertension, neurodegenerative disorders.

Acknowledgements: none

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